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Prevention or Treatment? The Case of Malaria.*

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Abstract

We present a simple theoretical model of household preventive behavior in response to malaria prevalence. The novelty is to include a trade-off between prevention and treatment in an otherwise standard epidemiological model of disease transmission, which depends on the relative price of treatment with respect to prevention. A relatively low price of treatment reduces protection.

Keywords: : Economic epidemiology, Malaria, Treatment, Prevention, Price

JEL: O12, I15, I25

1 Introduction

In spite of the recent decreases in malaria mortality and morbidity (Feachem et al., 2010; Jamison et al., 2013), this disease persists in large regions of the world. This can be partly explained by the high heterogeneity in disease environment. Furthermore, the relationship between economic development and malaria elimination follows a bidirectional relationship, which has been extensively discussed in the economic literature. Long-lasting insecticidal nets (LLINs) have been shown to be efficient preventive tools leading to ambitious campaigns of LLINs dissemination. However, in spite of their mechanical and chemical efficiency, LLINs are partially used by the populations and the efficiency decreases through time. This hinders malaria elimination. A malaria trap defined as the result of malaria reinforcing poverty, while poverty reduces the ability to control malaria, has been found to be one possible explanation for such paradox (Berthélemy et al., 2013).

A review of studies on price-elasticity of health products (Bates et al., 2012), including malaria specific measures, shows that charging small fees in an attempt to balance access and "sustainability" may not be a good solution, as relative to free distribution, charging even very small user fees is highly disincentivizing. Behavioral obstacles to elimination of malaria also appear to have been underestimated. LLINs reduced malaria transmission and child morbidity in short-term trials. However, it has been shown (Rhee et al., 2005; Toé et al., 2009) that, even in experimental contexts, the use of bednets remained low.

The second strategy, which has been involved in the malaria burden decrease, is the access improvement to rapid diagnostic tests (RDT) and treatment. Actually, artemisinin-based chemotherapy (ACT) are very efficacious, in spite some cases of resistances in Asia (Tulloch et al., 2013). Many countries have pushed up elimination policies based on free access to ACT. Different studies have studied the impact of the RDT use or knowledge on behaviors (Cohen, Dupas and Schaner, 2012; Adhvaryu, 2014) showing that many patients are taking ACT even with negative RDT. All studies recommend to improve both LLIN use and ACT access. But, none have studied the impact of treatment-based policies on LLIN use.

In this paper, we present a simple theoretical model of preventive and treatment behavior related to malaria prevalence. The framework follows the economic epidemiology literature (Philipson, 2000; Gersovitz and Hammer, 2003, 2004, 2005). The novelty is to

include a trade-off between prevention and treatment which depends on the relative cost of treatment with respect to prevention. Such behavioral response was also observed following the introduction of ARV treatments in the US in 1996 (Geoffard and Méchoulan, 2004). In this context, the benefit that is associated with the scaling-up of ARV treatments in terms of a decreased number of new infections could be at least partly offset by a relapse in the preventive behaviors among the general population. In extreme scenarios, the number of new infections could increase after a larger diffusion of ARV treatments, similar to what has been modeled for the hypothetical release of a vaccine (Blower and McLean, 1994; Bogard and Kuntz, 2002).

The rest of this paper is organized as follows. Section 2 briefly describes the epidemiological framework. Protection and treatment are added in 3 and 4. Section 5 outlines the main implications.

2 Standard epidemiological model of malaria transmission

A classical approach was used to model transmission of malaria between human populations and mosquito (*Anopheles*) populations (Smith and McKenzie, 2004), based on the McDonald and Ross malaria transmission model. The following classical assumptions have te be beared for both human and mosquito populations: constant population sizes through time, uniform contacts, no superinfection or immunity. The time variation of malaria prevalences among human (eq.1) and mosquito (eq.2) populations are defined as follow:

$$\dot{X} = mabZ(1 - X) - rX \tag{1}$$

$$\dot{Z} = acX(e^{-gn} - Z) - gZ \tag{2}$$

where m is the mosquito density (ratio of mosquitoes per human), a is the number of bits per unit of time and per mosquito, b is the proportion of infected bites that produce infection among humans, Z is the proportion of infectious mosquitoes, r is the clearance rate of malaria in humans, c is the proportion of bites on infectious humans that produce transmission to

mosquitoes, g is the death rate of mosquitoes, and n is the length of sporogonic cycle.

Assuming that the life-time period of humans is long enough, malaria prevalence reaches a steady state equilibrium defined by a concave function Q(X, m) (see Berthélemy et al. (2013)), for which the slope at origine is the basic reprodution rate, R_0, and:

$$\begin{cases} Q(0,m) = 0, \\ Q(1,m) < 1 \end{cases} \tag{3}$$

The function $Q(X,m)$ converges towards the trivial disease free stable steady state, if $R_0 \leq 1$. This case is not considered in what follows, as it does not coincide with the persistence of malaria in large regions of the developing world. Conversely, $Q(X,m)$ converges towards a stable steady state characterized by a strictly positive prevalence of malaria.

3 Economic epidemiological model with protection

The aim of LLIN-based policies is that protection tools such as LLIN could reduce malaria transmission, leading to a disease free stable steady state. But these policy only address the problem of LLIN distribution but rarely the LLIN use. Protection behavior has been added to the previous epidemiological transmission model, based on economic mechanisms and fully described in Berthélemy et al. (2013). Two protective behaviors are defined: LLIN use ($h = 1$) or no use ($h = 0$) leading to malaria exposure. It was assumed that the only mean to prevent from infection is to use a LLIN, LLIN use was supposed to provide complete protection. These assumptions can be relaxed without affecting the main findings of the model (Berthélemy et al., 2013). At any time, depending on the use of LLIN before, the health status of the individual, can be susceptible, $\sigma(h) = S$, or infected, $\sigma(h) = I$. The probability of being infected at any time, conditionally to the absence of protection before, can then be written as:

$$\pi_I = P(\sigma(h) = I | h = 0) = Q(X,m) \tag{4}$$

and then:

$$X = (1 - H)\pi_I \tag{5}$$

where H is the proportion of LLIN use among $(1-X)$ uninfected.

The mosquito density, m, is modified by LLIN use: the exposed human population decreased, being only the proportion $1-H$ of non-protected population; the absolute number of mosquitoes decreases with H as LLINs kill mosquitoes (knock down effect). Hence m, which was a parameter in the pure epidemiological model, can be written as a function of H as follows :

$$m(H) = \frac{m(0)}{1-H}(1-\gamma(H)) \tag{6}$$

where $\gamma(H)$ is the proportion of mosquitoes killed by LLINs, an increasing function of H, and $m(0)$ is the value of mosquito density in case of no protection. It follows that, at the steady state, $Q(X, m(H)$, and then the probability of being infected pi_I depend on H.

At the microeconomic level, the choice of protection is determined by maximizing the expected utility of each individual. The decision h of protection affects individuals' utility through two path: (i) an expected positive impact on the health status in case of protection and (ii) a private cost, called κ. Protection decision is described through the following maximization program:

$$max_h E[u(\sigma(h))] - \kappa W(\omega)h \tag{7}$$

where $u(S)$ or $u(I)$ are the utility levels attached to the health status (susceptible or infected thus depending on h, the use of a protection), with $0 < u(I) < u(S)$; ω is the individual income; $W(\omega)$ is the marginal utility of the income, supposed as usual to decrease with income. The expected utility (the expected positive impact of using LLIN on the health status) can be estimated using the following probabilities of being susceptible or infected, conditionally to the use of protection:

$$\begin{cases} P(\sigma(h) = S|h = 1) = 1, \\ P(\sigma(h) = S|h = 0) = 1 - \pi_I, \\ P(\sigma(h) = I|h = 0) = \pi_I. \end{cases} \tag{8}$$

As in standard economic epidemiological models, the individual will use protective tools when $W(\omega)$ is lower than the expected utility loss associated with the risk of infection that

occurs in the absence of protection:

$$E[u(\sigma(1)) - u(\sigma(0))] \geq \kappa W(\omega)h \tag{9}$$

Thus protection occurs if and only if:

$$\pi_I \geq \frac{\kappa W(\omega)}{u(S) - u(I)} \tag{10}$$

Indeed, a person will use LLIN if the utility of being non-infected is greater than the utility of paying for a protective tool, according to the income and the probability of being infected without using any protection.

The key point in this approach is that the threshold probability of infection depends on the marginal income utility loss associated with using the LLIN, $\kappa W(\omega)$. The threshold function, linking π_I to ω, termed $C(\omega)$, is monotonic and $C'(\omega) < 0$. In addition, the function $C()$ is increasing with κ. Consequently:

$$\begin{cases} h = 1 \text{ if } \omega \geq C^{-1}(\pi_I), \\ h = 0 \text{ else} \end{cases} \tag{11}$$

and the income threshold conditioning protection, $C^{-1}(\pi_I)$, decreases with κ. Knowing individual protection behaviors, the percentage of protected persons can be computed as follows:

$$H = \int_{C^{-1}(\pi_I)}^{+\infty} f(\omega)d\omega \tag{12}$$

where f is the probability density function of ω, describing the income distribution of the population. The long term properties of the model are described in Berthélemy et al. (2013). In the next section, we include treatment in addition to prevention.

4 Economic epidemiological model with protection and treatment

Until now, we have focused on the dynamics without the presence of a treatment choice. Assuming that an infected individual can buy medical treatment at a unit cost, χ, which reduces his/her illness, then the treatment does not play exactly the same role as protection. There are two scenarios.

- Firstly, malaria chemoprophylaxis is a preventive measure and can be assimilated to the use of ITNs/LLINs in the model rather than to curative measures.
- Secondly, curative measures (or medical treatment in this case) will not play the same role as protection by ITNs in the model.

Treatment does not have an immediate effect on the infectious status of the individual but the decision tree changes as, in subsequent period, the infected individual will decide whether to buy medical treatment or not. The decision can be considered sequential, given that the decision to buy medical treatment is only taken once infection has been observed. However, the possibility of buying medical treatment will affect the protection decision before infection. A decision variable η, is therefore introduced, which is equal to 1 if the individual buys medical treatment and 0 if he/she does not.

In the subsequent period the treatment decision is represented as:

$$\eta = 1 \text{ if and only if } u(I|\eta = 1) - u(I|\eta = 0) \geq \lambda W(\omega) \tag{13}$$

where $u(I|\eta = 0)$ is the value of the health status when infected and non-treated, $u(I|\eta = 1)$ is the value of the health status when infected and treated, with $u(I|\eta = 0) \leq u(I|\eta = 1)$. λ is the unit cost of the treatment. An individual is susceptible after the treatment but the value of health is different from $u(S)$ as the individual has been sick, so that $u(S) > u(I|\eta = 1)$.

There are now two thresholds on π_I, depending on the value of η , denoted $C_\eta(\omega)$, with $\eta = 0$ or $\eta = 1$.

The condition given in equation (13) can be written as:

$$\eta = 1 \text{ if and only if } \omega \geq W^{-1}\left(\frac{u(I|\eta=1) - u(I|\eta=0)}{\lambda}\right) \tag{14}$$

For simplicity reason, the right-hand side expression is denoted ω_1. It depends only on parameters of the model (values attached to different health status) and on the price of the treatment. The higher the price of treatment, the higher ω_1, and the smaller the number of infected individuals who will decide to buy the treatment.

Once this second period decision rule has been established, an individual will choose in the first period to use the protection device according to a rule comparable to that of the previous section,

$$h = 1 \text{ if and only if } \omega \geq C_\eta^{-1}(\pi_I) \text{ for } \eta = 0 \text{ or } 1 \tag{15}$$

where $C_0(\omega) = \frac{\lambda W(\omega)}{u(S)-u(I|\eta=0)}$ and $C_1(\omega) = \frac{\lambda W(\omega)}{u(S)-u(I|\eta=1)}$.

The complete solution then depends on how ω_1, $C_0^{-1}(\pi_I)$ and $C_1^{-1}(\pi_I)$ compare. From $u(I|\eta=0) \leq u(I|\eta=1)$, it can be inferred that $C_0^{-1}(\pi_I) \leq C_1^{-1}(\pi_I)$, $\forall \pi_I$. Then, there are only three cases to consider:

- *Case 1:* $\omega_1 \leq C_0^{-1}(\pi_I) \leq C_1^{-1}(\pi_I)$
- *Case 2:* $C_0^{-1}(\pi_I) \leq \omega_1 \leq C_1^{-1}(\pi_I)$
- *Case 3:* $C_0^{-1}(\pi_I) \leq C_1^{-1}(\pi_I) \leq \omega_1$

For *case 1*, $h = 1$ implies $\eta = 1$ and is obtained if and only if $C_1^{-1}(\pi_I) \leq \omega$, implying:

$$H = \int_{C_1^{-1}(\pi_I)}^{+\infty} f(\omega)d\omega, \text{ denoted } H_1(\pi_I). \tag{16}$$

For *case 2*, $h = 1$ either when $C_1^{-1}(\pi_I) \leq \omega$ (and $\eta = 1$) or when $C_0^{-1}(\pi_I) \leq \omega \leq \omega_1$ (and $\eta = 0$), then:

$$H = H_1(\pi_I) + \int_{C_0^{-1}(\pi_I)}^{\omega_1} f(\omega)d\omega \tag{17}$$

For *case 3*, $h = 1$ when $C_0^{-1}(\pi_I) \leq \omega$ (and $\eta = 0$), then:

$$H = \int_{C_0^{-1}(\pi_I)}^{+\infty} f(\omega)d\omega, \text{ denoted } H_0(\pi_I). \tag{18}$$

Given the definitions of $H_0(\pi_I)$ and $H_1(\pi_I)$ it is clear that $H_1(\pi_I) \leq \mathrm{H}_0(\pi_I)$. Overall, H can be represented as a function of π_I as illustrated in Figure 1. This function of π_I is continuous everywhere but not differentiable at $C_0(\omega_1)$ or $C_0(\omega_1)$. For $\pi_I \in [0, C_0(\omega_1)[$, its partial derivative is equal to:

$$\frac{\delta H}{\delta \pi_I} = \frac{f(C_1^{-1}(\pi_I))}{C_1'(\pi_I)} \tag{19}$$

while for $\pi_I \in [C_0(\omega_1), C_1(\omega_1)]$, its partial derivative is equal to:

$$\frac{\delta H}{\delta \pi_I} = \frac{f(C_1^{-1}(\pi_I))}{C_1'(\pi_I)} - \frac{f(C_0^{-1}(\pi_I))}{C_0'(\pi_I)} \tag{20}$$

and for $\pi_I \in [C_1(\omega_1), +\infty[$, its partial derivative is equal to:

$$\frac{\delta H}{\delta \pi_I} = \frac{f(C_0^{-1}(\pi_I))}{C_0'(\pi_I)} \tag{21}$$

Figure 1 illustrates how the model changes in relation with the introduction of a possible treatment. Specifically, it introduces changes in the protection behavior depending on the price of treatment λ.

When the price of treatment, λ, increases, ω_1 increases and $C_0^{-1}(\pi_I)$ and $C_1^{-1}(\pi_I)$ decrease. If the price is very high or very low, the kinks of Figure 1 are moved leftward or upward. For a price equal to 0 or infinite, they disappear.

5 Conclusions

The main conclusions of the model are the following. First, a low price of treatment (*case 1*) implies that individuals will buy treatment in case of infection, and $H = H_1(\pi_I)$. As a consequence there is less protection than in absence of a treatment, but protective behaviors are locally invariant with λ.

Second, An intermediate price of treatment (*case 2*) implies that some, but not all, infected individuals buy treatment. As a consequence there is less protection than in absence

of a treatment, and protective behaviors depends positively on λ.

Third, a high price of treatment (*case 3*) implies that individuals do not buy treatment when they are infected, and $H = H_0(\pi_I)$. As a consequence the protective behavior is locally the same as in absence of treatment.

Calibrating the model with known parameters from the literature constitutes avenues for future research. This could enable us to show how the results generate different predictions regarding the equilibrium levels of infection and the usage of treatment and prevention from epidemiological models which do not take this tradeoff explicitly into account.

References

Adhvaryu, Achyuta. 2014. "Learning, Misallocation, and Technology Adoption: Evidence from New Malaria Therapy in Tanzania." *The Review of Economic Studies*, rdu020.

Bates, Mary Ann, Rachel Glennerster, Kamilla Gumede, and Esther Duflo. 2012. "The Price is Wrong." *Field Actions Science Reports. The journal of field actions*, , (Special Issue 4).

Berthélemy, Jean-Claude, Josselin Thuilliez, Ogobara Doumbo, and Jean Gaudart. 2013. "Malaria and protective behaviours: is there a malaria trap?" *Malaria journal*, 12(1): 200.

Blower, S. M., and A. R. McLean. 1994. "Prophylactic vaccines, risk behavior change, and the probability of eradicating HIV in San Francisco." *Science (New York, N.Y.)*, 265(5177): 1451–1454.

Bogard, Elizabeth, and Karen M. Kuntz. 2002. "The impact of a partially effective HIV vaccine on a population of intravenous drug users in Bangkok, Thailand: a dynamic model." *Journal of Acquired Immune Deficiency Syndromes (1999)*, 29(2): 132–141.

Cohen, Jessica, Pascaline Dupas, and Simone G. Schaner. 2012. "Price subsidies, diagnostic tests, and targeting of malaria treatment: evidence from a randomized controlled trial." National Bureau of Economic Research.

Feachem, Richard GA, Allison A Phillips, Jimee Hwang, Chris Cotter, Benjamin Wielgosz, Brian M Greenwood, Oliver Sabot, Mario Henry Rodriguez, Rabindra R Abeyasinghe, Tedros Adhanom Ghebreyesus, and Robert W Snow. 2010. "Shrinking the malaria map: progress and prospects." *The Lancet*, 376(9752): 1566–1578.

Geoffard, Pierre-Yves, and Stéphane Méchoulan. 2004. "Comportements sexuels risqués et incitations." *Revue économique*, 55(5): 883–899.

Gersovitz, Mark, and Jeffrey S. Hammer. 2003. "Infectious diseases, public policy, and the marriage of economics and epidemiology." *The world bank research observer*, 18(2): 129–157.

Gersovitz, Mark, and Jeffrey S. Hammer. 2004. "The Economical Control of Infectious Diseases*." *The Economic Journal*, 114(492): 1–27.

Gersovitz, Mark, and Jeffrey S. Hammer. 2005. "Tax/subsidy policies toward vector-borne infectious diseases." *Journal of Public Economics*, 89(4): 647–674.

Jamison, Dean T., Lawrence H. Summers, George Alleyne, Kenneth J. Arrow, Seth Berkley, Agnes Binagwaho, Flavia Bustreo, David Evans, Richard GA Feachem, Julio Frenk, and others. 2013. "Global health 2035: a world converging within a generation." *The Lancet*, 382(9908): 1898–1955.

Philipson, Tomas. 2000. "Economic epidemiology and infectious diseases." *Handbook of health economics*, 1: 1761–1799.

Rhee, Michelle, Mahamadou Sissoko, Sharon Perry, Willi McFarland, Julie Parsonnet, and Ogobara Doumbo. 2005. "Use of insecticide-treated nets (ITNs) following a malaria education intervention in Piron, Mali: a control trial with systematic allocation of households." *Malaria Journal*, 4(1): 35.

Smith, David L., and F. Ellis McKenzie. 2004. "Statics and dynamics of malaria infection in Anopheles mosquitoes." *Malaria Journal*, 3(1): 13.

Toé, Léa Paré, Olé Skovmand, Kounbobr Roch Dabiré, Abdoulaye Diabaté, Yveline Diallo, Tinga Robert Guiguemdé, J. M. Doannio, Martin Akogbeto, Thierry Baldet, and Marc-Eric Gruénais. 2009. "Decreased motivation in the use of insecticide-treated nets in a malaria endemic area in Burkina Faso." *Malar J*, 8: 175.

Tulloch, Jim, Benedict David, Robert D. Newman, and Sylvia Meek. 2013. "Artemisinin-resistant malaria in the Asia-Pacific region." *The Lancet*, 381(9881): e16–e17.

Figure I: Treatment and prevention